For a teaching of applicants' "receptor I" the Examiner cites paragraph [0079], lines 43-60, at page 8 of the Niemeyer et al. As noted by the undersigned in the interview, one problem presented by the Examiner's reliance upon paragraph [0079], lines 43-60 of Niemeyer et al for disclosure of applicants' "receptor I" is that the teaching cited by the Examiner actually describes two significantly different assays, both of which are significantly different from that shown schematically in Fig. 5. One assay is that described in paragraph [0079] at lines 43-54. A second, substantially different assay, is described at paragraph [0079] at lines 54-60 beginning with the word "Alternatively". Here reference is made to "Attachment C" where paragraph [0079] is reproduced with insertions of schematics illustrating the two assays. Referring to paragraph [0079] the Examiner writes:

> "Niemeyer et al disclose that this conjugated compound [allegedly, "receptor I"] comprises biotinylated (B1) antibody (L1) combined with streptavidin (R1) coupled to nucleic acid (M) (p.8, para. 0079, lines 43-60)."

The Examiner's characterization of an alleged "receptor I" quoted above would seem to match, in part, the antibody-nucleic acid conjugate used in the second, alternative assay described in lines 54-60 of paragraph [0079], which "antibody-nucleic acid conjugate" is shown as reactant "B" in the assay (II) of Attachment C. However, the Examiner's description of a "receptor I" does not fit the definition of receptor I in applicants' claims where receptor I is defined as having a bound marker "M". In the alternative assay II in paragraph [0079], the "label" is the marker, not the "complimentary nucleic acid" to which it is "connected." Note in the assay II described at lines 54-60 in paragraph [0079], the "antibody-nucleic acid conjugate" (reactant B) is added to the sample prior to addition of the "label connected to a complimentary nucleic acid." Thus, unlike applicants' "receptor I" the antibody-nucleic acid conjugate (reactant B) of the "alternative" assay II does not include a marker "M". The "antibody-nucleic acid conjugate" (reactant B) in the alternative assay II of paragraph [0079] would

correspond to what the Examiner has identified as "receptor II", if reactant B were to have a single nucleic acid strand as does "receptor II" of the embodiment of Fig. 5. Referring to attachments A-C, while the "label connected to a complimentary nucleic acid" (compound D) may be the equivalent of the antibody-enzyme conjugate in the assay of Fig. 5 (compound X), the "antibody-nucleic acid conjugate" (compound B) certainly is not. Summarizing, while the alternative assay II of paragraph [0079] includes compounds B and D, roughly equivalent to, respectively, "receptor II" and compound X in Fig. 5, as described in paragraph [0127], neither assay II nor that of Fig. 5 includes any reactant the equivalent of applicants' "receptor I" and, accordingly, no conceivable combination of such assays can yield an assay within the scope of applicants' claims.

Turning now to the first assay (I) described in paragraph [0079] at lines 43-54, a biotinylated antibody (designated compound E on attachment C) is first added to the sample to capture the target analyte. Note that compound A might satisfy applicants' definition of receptor I, but for the fact that it has no group which is capable of binding with the analyte. Also note that assay I of [0079] uses no reagent corresponding to applicants' receptor II. It should be self-evident that compound A of assay I cannot be substituted for the antibody-enzyme conjugate (compound X) of the assay of Fig. 5 because, unlike the antibody of compound X, there is no group in compound A capable of binding with the analyte. Compound A of assay I more closely corresponds to a sub-combination within "receptor II" of the assay of Fig. 5.

The Examiner's attempt to somehow combine teachings of different assays in paragraph [0079] with the assay of Fig. 5 is also considered erroneous because the assay of Fig. 5 is described in paragraph [0127] as a "sandwich ELISA" (lines 13-15), as can be clearly seen in Fig. 5 itself. Thus, in Fig. 5 the target analyte becomes sandwiched between the antibody of the antibody-enzyme conjugate "X" and the antibody of "receptor II". In contradistinction, neither of assays I and II described in paragraph [0079] is a "sandwich" type assay. Accordingly, it is

respectfully submitted that the Examiner is erroneously attempting to combine reagents from three very different types of assays.

Parenthetically, in paragraph 4 of the office action the Examiner refers to "a target analyte such as an antibody" citing paragraph [0127], lines 11-13. However, the analyte described there is an antigen. "The translated DNA array was used to bind specifically IgG antigens from a mixture of possible IgG targets."

The rejection, as applied to claim 28, is further traversed. With regard to claim 28 the Examiner writes:

> "With respect to claim 28, Niemeyer et al discloses that the receptor I and receptor II are different reagents and used in a sequential manner and thus one of ordinary skill in the art would recognize that the reagents are separate within the kit of Niemeyer et al."

It is respectfully submitted that the Examiner's factual premise is erroneous. As noted above, Niemeyer et al nowhere disclose any assay using both a receptor I and receptor II, much less such use in a sequential manner.

The rejection of claims 4-7 and 19 for obviousness, as set forth in paragraph 5 of the office action, is respectfully traversed for substantially the same reasons given above. Applicants acknowledge the proposition for which the Examiner cites Bayer et al and, indeed, show strepavidin in attachment C as having four binding points. However, the additional citation of Bayer et al in no way cures the deficiencies of Niemeyer et al noted above.

The rejection of claim 12 for obviousness over Niemeyer et al in view of Ghosh et al is traversed for substantially the same reasons given above. Changing the analyte to a nucleic acid and the antibodies to oligonucleotides in, for example, the assay of Fig. 5 of Niemeyer et al, would not yield an assay inclusive of applicants' "receptor I".

The rejection of claims 15 and 17 for obviousness over Niemeyer in view of Billing-Medel et al is not understood. Apparently, the Examiner relies upon Billing-Medel et al for their teaching of "the use of antigen/antibody pairs". However, the assay of Fig. 5 of Niemeyer et al employs antigen-antibody coupling and,

accordingly, it is not understood how the additional citation of Billing-Medel et al adds anything of relevance to the teachings of Niemeyer et al.

Finally, the rejection of claims 26 and 27, as set forth in paragraph 8 of the office action is traversed. The Examiner relies upon the additional citation of the Millipore publication for a teaching of formation of lines on a membrane in detecting the analyte. However, the Millipore publication does nothing to cure the deficiencies of Niemeyer et al noted above.

ADVNATAGES OF THE PRESENT INVENTION

Applicants also wish to emphasize that claim 1 and the claims dependent thereon, directed to a "kit", define a solid phase conjugate as being contained in the kit "separate from at least receptor II." Such a kit offers the following advantages neither appreciated nor suggested by Niemeyer et al.

1. Advantage of a reduced number of washings with the kit and process of the present invention.

If the Receptor II (L2-B2-R2-B3) and the solid phase conjugate (R3-Solid phase) were contained together in the kit, B3 and R3 both of which have mutual affinity, would be bonded to each other in the analyte detection process to form another solid phase conjugate composed of L2-B2-R2-B3-R3-Solid phase, requiring a first washing. Secondly, after the first washing step, an analyte A would be bonded to the resulting solid phase conjugate to form still another solid phase conjugate composed of A-L2-B2-R2-B3-R3-Solid phase, requiring a second washing. Thirdly, after the second washing step, the Receptor I (L1-B1-R1-M) would be bonded to the resulting solid phase conjugate to form a further solid phase conjugate composed of M-R1-B1-L1-A-L2-B2-R2-B3-R3-Solid phase, requiring a third washing. Finally, after the third washing, a label would be detected in the final resulting conjugate bound to solid phase.

In contrast, in the present invention where the solid phase conjugate (R3-Solid phase) is stored separately from the Receptor II in the kit, in the analyte detection process, after the Receptor I (L1-B1-R1-M) and the Receptor II (L2-B2-R2-B3) have reacted or while reacting with at least a bivalent analyte A to form a

solid phase conjugate composed of M-R1-B1-L1-A-L2-B2-R2-B3, the resulting conjugate reacts with another solid phase conjugate (R3-Solid phase) to form still another solid phase conjugate composed of M-R1-B1-L1-A-L2-B2-R2-B3-R3-Solid phase. After the first washing step has been finished, the label in the bound conjugate is detected.

Thus, the kit of the present invention offers the advantage that its use requires only one washing step, allowing for easier detection or quantifying in less time.

2. Advantage of being capable of using the same solid phase conjugate to detect or measure any of various analytes.

If the Receptor II (L2-B2-R2-B3) and the solid phase conjugate (R3-Solid phase) are together in the kit, the solid phase conjugate composed of L2-B2-R2-B3-R3-Solid phase would be formed. The resulting solid phase conjugate has a specific ligand (L2) bonded. On the other hand, separately from the solid phase conjugate (R3-Solid phase) in the kit, an agent containing the Receptor II may be designed at the discretion of the manufacturer as occasion demands. This means that simply by changing L2 in the Receptor II (L2-B2-R2-B3) in accordance with the analyte A to be detected, various analytes A may be easily assayed with the solid phase conjugate (R3-Solid phase) unchanged.

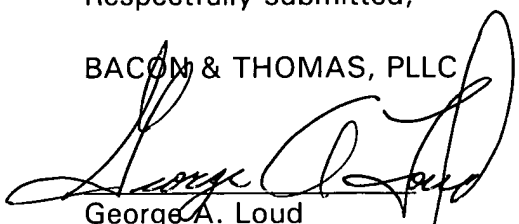
3. Advantage of being capable of omitting a binding step in the kit fabrication.

To store the Receptor II (L2, B2, R2, B3) and the solid phase conjugate (R3-Solid phase) together in the kit in the form of a solid phase conjugate composed of L2-B2-R2-B3-R3 Solid phase, manufacturers would be required to execute an extra manufacturing step, namely a binding step. However, the present invention, wherein the Receptor II (L2-B2-R2-B3) and the solid phase conjugate (R3-Solid phase) are stored in the kit separately from each other, the need for such an additional (binding) step is eliminated.

In conclusion, it is respectfully requested that the Examiner reconsider the rejections of record with a view toward allowance of the pending claims.

Respectfully submitted,

BACON & THOMAS, PLLC



March 6, 2006
Date

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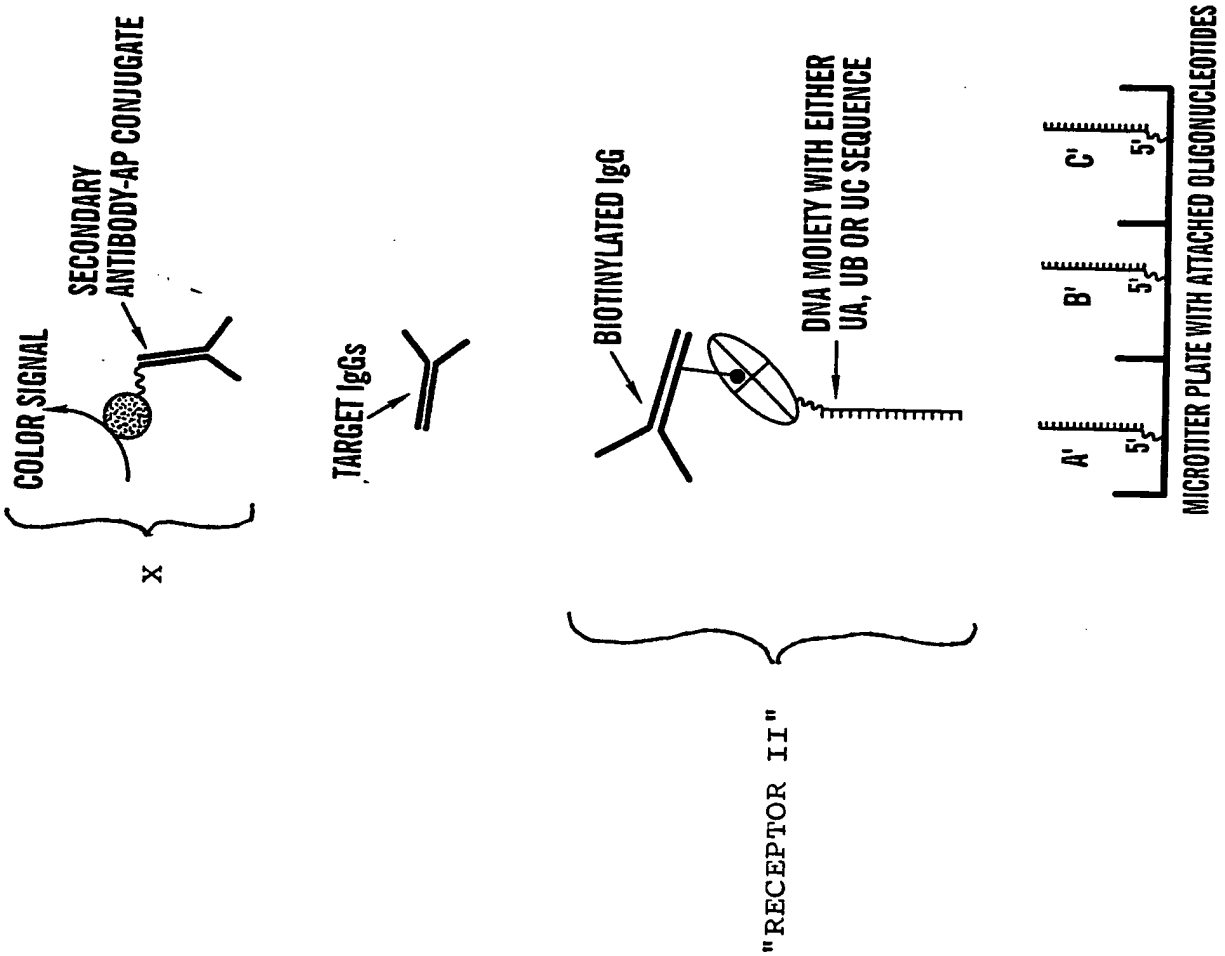
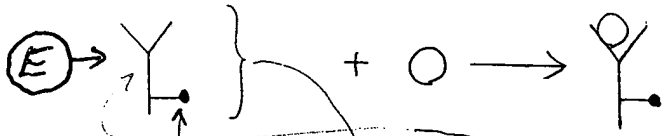
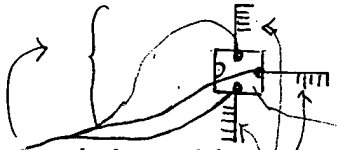
ATTACHMENT "B"



[0079] Another embodiment of the invention is directed to in vitro methods for detecting a target in a sample.



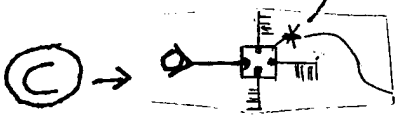
For example, one method comprises the steps of conjugating an antibody specific for the target with biotin and adding the conjugated antibody to the sample.



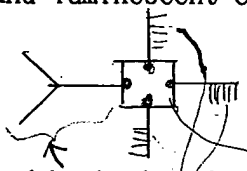
I

A multimeric nucleic acid construct is prepared comprising one or more biotinylated single-stranded nucleic acids bound to streptavidin.

The construct is labeled with a detectable label and the labeled construct added to the sample.



Examples of detectable labels include radio isotopes, stable isotopes, enzymes, fluorescent and luminescent chemicals, chromatic chemicals, metals mid electrical charges.



II

Alternatively, the biotinylated antibody may be combined with streptavidin coupled to a particular nucleic acid before addition to the sample.

After the antibody-nucleic acid conjugate is added to the sample, bound antibody can be detected by the addition of a label connected to a complementary nucleic acid.